each of k, l, and m is independently zero or an integer from 1 to 5;

p is zero or 1;

R^h is OH, NH_2 or -NHLysNH$_2$; and

R^i is H or $COCH_3$.--

REMARKS

Claims 1-8 and 11-21 are pending in this patent application. Added claims 11-21 find support, for example, in the specification at pages 9-12 and in original claims 2-8, and are not believed to introduce new matter. Applicants hereby affirm the provisional election of claims 1-8 which had been made in response to the requirement for restriction.

The Office Action objects to the sequence listing which was filed with this patent application in view of a number of perceived informalities in the computer readable form thereof. Enclosed herewith is a replacement copy of the computer readable form which is believed to address these informalities.

Claims 1-8 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Applicants respectfully request reconsideration of this rejection, as it is undisputed that those skilled in the art would be able to practice the claimed inventions. The inventions defined by claims 1-8 relate, in part, to nucleic acid mimics comprising a non-naturally occurring backbone to which are appended a plurality of heterocyclic bases.

An exceedingly wide variety of compounds having non-naturally occurring backbones and heterocyclic bases are known (*see, e.g.*, pages 2-3 of WO 86/05518, which already is of record), and there is no reason to believe that those skilled in the art would not be able to adapt each of these compounds to include the sterically bulky substituents required by the claims. Indeed, the Office Action is in agreement on this point, as it acknowledges that those skilled in the art would be able to practice the claimed inventions without undue experimentation with any of the backbones "that are either well known in the art or described in significant detail in the instant specification." (Office Action at page 5). The Office Action suggests that the reactivity of nucleotide bases makes the determination of synthetic pathways to nucleic acid mimics "complex." (*id.*). Significantly, however, there is no reason to believe that those skilled in the art are not able to successfully address this perceived complexity. Indeed, the variety and number of non-natural backbone structures which are already known is telling, objective evidence that the reactivity of nucleotide bases would ***not*** prevent those skilled in the art from preparing the claimed compounds. In view of this evidence, reconsideration and withdrawal of the rejection for alleged lack of enablement respectfully is requested.

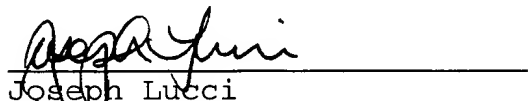
Claims 1-8 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by WO 86/05518 ("the Summerton reference"). Applicants respectfully request reconsideration of

this rejection, as the Summerton reference neither discloses nor suggests the claimed inventions. The Summerton reference has been asserted to disclose certain synthetic intermediates which have a non-natural backbone and bear protecting groups on nucleosidic bases. Synthetic intermediates, however, are not within the scope of claims 1-8, and Applicants have amended the claims to even more clearly define their invention in this regard by reciting both mimics and target molecules. This amendment finds support in the specification at, for example, page 15, lines 27-35 and page 16, line 34 - page 17, line 19. Because the compounds disclosed by the Summerton reference are mere synthetic intermediates, the reference fails to so much as suggest the claimed mimics in admixture with the recited target molecules. In view of this clear deficiency in the teaching of the Summerton reference, Applicants request that the rejection for alleged anticipation be reconsidered and withdrawn.

In view of the foregoing, Applicants submit that the claims presently before the Examiner patentably define the

invention over the applied art and are otherwise in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,



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Date: May 5, 1997

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independently selected from the group consisting of hydrogen, $(C_2$-$C_6)$alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylthio, NR^3R^4 and SR^5, where R^3 and R^4 independently are hydrogen, a conjugate, $(C_1$-$C_4)$alkyl, hydroxy- or alkoxy- or alkylthio-substituted $(C_1$-$C_4)$alkyl, hydroxy, alkoxy, alkylthio or amino; and R^5 is hydrogen, $(C_1$-$C_6)$alkyl, hydroxy-, alkoxy-, or alkylthio- substituted $(C_1$-$C_6)$alkyl, or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

each of D^1-D^n is $(CR^6R^7)_z$ where R^6 and R^7 are as defined above;

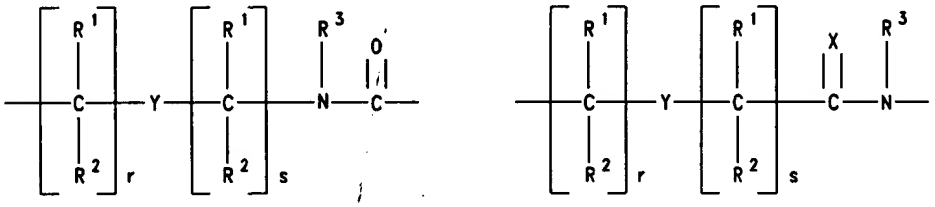
each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

each of G^1-G^{n-1} is $-NR^3CO-$, $-NR^3CS-$, $-NR^3SO-$ or $-NR^3SO_2-$, in either orientation, where R^3 is as defined above;

each pair of A^1-A^n and B^1-B^n are selected such that:

(a) A is a group of formula (IIc) and B is N or R^3N^+; or

(b) A is a group of formula (IId) and B is CH;



(IIc) (IId)

where:

X is O, S, Se, NR^3, CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4;

REMARKS

Claims 1-8 and 11-21 are pending in the application. The amendment to the specification with respect to variables R^3 and R^4 finds support, for example, at page 8, lines 22-25 of application Serial No. 08/319,411, the contents of which are incorporated into the present patent application (*see*, page 3, line 33 - page 4, line 6).

The Office Action objects to the instant application due to alleged non-compliance with the requirements for sequence listings as set forth in 37 CFR §1.821(a)(1) and (a)(2). Specifically, it is asserted that the specification on pages 19 and 21 contains sequences without SEQ ID NOS. Applicants herein amend the specification to include the SEQ ID NOS for the sequences present on pages 19 and 21 to further clarify the invention. Support for these amendments may be found on page 20, lines 11-17 and page 22, lines 8-12.

Claims 1-8 stand rejected under 35 U.S.C. §112, first paragraph. Although the Examiner suggested certain limitations in a previous Office Action, the Examiner now alleges there to be insufficient written basis for such limitations. Applicants do not concur, but note that these claims have been canceled to advance prosecution of the remaining claims.

Claims 11-21 stand rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly fails to describe admixtures containing a target molecule and a compound of the invention having, for example, amino protecting groups and activated derivatives of certain substituents. Applicants note, however, that the specification clearly discloses such admixtures in that it teaches: (1) that the "compounds of the present invention" can be used in methods that involve forming mixtures with a target molecule (*see, e.g.*, pages 15-17); and (2)

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that the compounds of the invention include, for example, "activated derivatives" (page 10, lines 17-18) and amino protecting groups (*see, e.g.*, page 10, lines 19-24). Accordingly, Applicants request that the rejections under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn.

Claim 13 stands rejected under 35 U.S.C. §112, second paragraph, as allegedly being unclear in its recitation of substituents having three or more atoms. Applicants have amended claims 2 and 13 to even more clear describe the claimed inventions. Support for this amendment may be found in the specification at, for example, page 6, lines 7-9.

Claims 11, 20 and 21 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly lacking proper antecedent basis for the functional groups R^3 and R^4. Applicants believe that this rejection is moot in view of the foregoing amendment of the specification and claims.

Claims 11-17, 20 and 21 stand rejected under 35 U.S.C. §103, as allegedly being unpatentable over U.S. Patent No. 5,705,333 ("the Shah patent") taken in view of either Webb, *et al., J. Am. Chem. Soc.* **1986**, *108*, 2764 ("the Webb reference"), Summerton *et al., J. Mol. Biol.*, **1978**, *122*, 145 ("the Summerton reference"), Inoue *et al., Nucleic Acids Research* **1985**, *13*, 7119 ("the Inoue reference"), or U.S. Patent No. 4,828,979 ("the Klevan Patent"). Applicants respectfully request reconsideration of this rejection, as combination of the cited references would not produce any claimed invention. The cited references, for example, do not appear to disclose or suggest any structure corresponding to formulas IIc and IId in claim 22. Thus, even if a person of ordinary skill would have been motivated to combine the teachings of these references (and Applicants do not believe that those of ordinary skill would have been so motivated), such a combination would not have produced any claimed invention. Accordingly,

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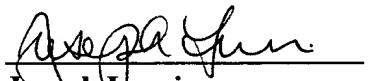
Applicants respectfully request the reconsideration and withdrawal of the rejection under § 103. *In re Payne*, 203 U.S.P.Q. 245, 255 (C.C.P.A. 1979) (references relied upon to support rejection under § 103 must place the claimed invention in the possession of the public).

It is believed all of the claims presently before the Examiner patentably define the invention over the prior art and are otherwise in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,



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